PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application No.	:	10/084,857 Confirmation No.: 6210
Applicant:	:	Jan Weber
Filed:	:	February 25, 2002
TC/A.U.	:	3731
Examiner:	:	Vy Q. Bui
Docket:	:	01-264US
Customer No.:	:	38356
Title:		Non-Invasive Heating of Implanted Vascular Treatment Device

Commissioner for Patents
P.O. BOX 1450
Alexandria, VA 22313-1450

DECLARATION OF DR. JAN WEBER UNDER 37 CFR §1.131

1. I, Jan Weber, Ph.D., am the inventor in the above-identified patent application. The present patent application is an original U.S. Patent Application filed on February 25, 2002.

2. I currently am employed by Boston Scientific SCIMED, Inc., a division of Boston Scientific Corp., having its place of business at One Scimed Place, Maple Grove, Minnesota 55311-1566. I have been employed by Boston Scientific Corp. for the seven years, the past four years with Boston Scientific SCIMED, Inc. I have also held the position of Manager of Advanced Research and Development at Cordis Europa in Roden, The Netherlands, from 1989 to 1998, and the position of Scientific Staff Member in the Department of Physics at the Free University of Amsterdam from 1987 to 1989.

With Boston Scientific Corp., I have held the position of Manager of Process Development (Boston Scientific, Ireland) from 1998 to 2001. I am currently a Director Level Senior Research Fellow with Boston Scientific SCIMED, Inc. (2001 to present). My research involves, among other things, the development and

application of new technologies from outside of Boston Scientific SCIMED, Inc. to potential future product applications for Boston Scientific SCIMED, Inc., with emphasis in the cardiovascular device technologies. I have numerous Published U.S. Patent Applications and issued U.S. Patents in this area.

3. I have reviewed U.S. Patent Number 6,786,904 to Doscher *et al.* cited by the Examiner in an Office Action mailed in the prosecution of U.S. Patent Application Serial No. 10/084,857 mailed on October 19, 2004. I make this Declaration in support of the patentability of the claims of U.S. Patent Application Serial No. 10/084,857.

4. U.S. Patent Number 6,786,904 to Doscher *et al.* (Doscher) was filed in the United States Patent and Trademark Office on January 10, 2002, as indicated by the cover page of the patent.

5. Prior to the January 10, 2002 filing date of U.S. Patent Number 6,786,904 to Doscher *et al.*, the inventor of the present U.S. Patent Application conceptualized the vascular treatment device claimed in the present patent application, and worked diligently to create the vascular treatment device and the method of their creation as claimed in the present patent application.

6. **Exhibits A and B** attached hereto and incorporated by reference herein, are submitted as factual evidence of conception of the invention in the United States prior to the filing date of U.S. Patent 6,786,904 to Doscher *et al.* coupled with due diligence from the conception in the United States to reduction to practice.

7. **Exhibit A** is submitted as factual evidence that the invention was conceived by the inventor in the United States prior to the filing date of U.S. Patent 6,786,904 to Doscher *et al.* (Doscher). **Exhibit A** is a photocopy of an Idea Disclosure Form used by the Boston Scientific Corporation. The pages describe the development of the vascular treatment device and vascular treatment system as claimed in the

present invention. The pages describe incorporating magnetically susceptible material with vascular treatment devices, as well as systems that utilize such devices. The magnetically susceptible materials have a magnetic susceptibility that decreases within a preselected temperature range. In particular, the magnetically susceptible materials could be selected so as to have a desired Curie temperature in the preselected temperature range.

8. **Exhibit B** is submitted as factual evidence that the invention was conceived by the inventor in the United States prior to the filing date of Doscher and diligently pursued from a time preceding the filing date of Doscher to its reduction to practice. **Exhibit B** is a photocopy of certain pages from a report on In Vitro Cytotoxicity. The report provides a biological evaluation of medical devices that include the magnetically susceptible materials of the present invention. In particular, the report indicates that no signs of reactivity were exhibited by L929 mouse fibroblast cells to the medical devices that include the magnetically susceptible materials of the present invention.

10. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that the statements are made with the knowledge that willful false statement and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

18 of February 2005.
Date

Jan Weber

Exhibit A

Boston Scientific Corporation

IDEA DISCLOSURE

Title of Idea: Non-Invasive heating of implanted arterial stents using incorporated FeO material.

BSC Division/Technology:

Date you begin filling out this form:

Key Words for Search: Curie point, restenosis prevention by heating

Innovator(s):	Name	Jan Weber, 763-494-2543 18112 89th Place N Maple Grove 55311, MN, (Dutch)	Work Location & Phone Ext, Home Address & Phone No. & Citizenship

1. _____
(Print/Type name as you would like it to appear on a Patent: generally, full name and middle initial)

Jan Weber _____
(Signature & Date)

2. _____
(Print/Type name as you would like it to appear on a Patent: generally, full name and middle initial)

_____
(Signature & Date)

3. _____
(Print/Type name as you would like it to appear on a Patent: generally, full name and middle initial)

_____
(Signature & Date)

Witnessed: DAN HORN _____

Date, Position & Extension: Mgr. APT x 1238

Witnessed: _____

Date, Position & Extension: _____

Boston Scientific Corporation

I. Description of Idea

1. *Briefly describe the current technology, devices, methods, etc. that relates to your idea and any disadvantages of the current technology. (Please attach any copies of articles, patents, drawings, pictures, brochures, presentations, instructions for use, etc. describing the current technology.)*

As was presented on the AHA

Quoted "

NON-INVASIVE HEATING OF IMPLANTED ARTERIAL STENTS IN VIVO: A NOVEL NEW METHOD TO PREVENT RESTENOSIS. FEASIBILITY AND SAFETY.

Leonidas D Diamantopoulos, Glenn Van Langenhove, David P Foley, Pim J De Feyter, Thoraxcenter, Rotterdam Netherlands Today, restenosis is the major complication of stent implantation. Heating of cells has been suggested as a method for inducing cell apoptosis. Methods: To heat the arterial wall in vivo, and thus increase cell apoptosis at the stent site, we developed a new method based on the capabilities of metals when placed inside an alternating magnetic field. Due to metallic stent retentivity, as the magnetizing force periodically changes, magnetic flux inside the stent lags behind.The result is a power loss to the magnetic circuit, which appears as heat in the metallic stent. Human and animal tissues are immune to hysteresis effects and losses, so they remain totally unheated. We constructed a high frequency alternating magnetic field generator, power-controlled by a PC computer with appropriate software. In a series of in-vitro tests we managed to heat several stents of the market in a human coronary artery model. Donor blood of 37oC, flow velocity 10-50cm/s and driving pressure 50-140mmHg was used to simulate the coronary flow. Fresh pork meat was placed around the arterial model. The temperature of the model was continuously monitored by an infrared thermal camera. In all experiments, stents were heated effectively up to 60oC, while the meat remained totally unheated. The histology of the unheated meat showed no evidence of thermal damages. The maintenance of stent temperature to levels of 43-45 oC was feasible by both power-algorithm and magnetic feedback techniques. Tests with nitinol stents verified remote expansion in all cases. Conclusions: This non-invasive method, that uses magnetic energy to heat metallic stents from a distance, is feasible and safe and may be used in the future after coronary stenting with the aim to reduce restenosis or for remote re-expansion of nitinol stents.

" End of quote

The disadvantage of this technology is that the heating is dependent on the change of magnetic flux through the stent, which is dependent on the alignment and positioning of the stent relative to the magnetic field lines.

Another disadvantage is that as the stents temperature is raised by the resistance to the electric currents induced by the change in flux, that the temperature rise is therefor not distributed homogeneous throughout the stent because of the effect that the stent is not a homogeneous tube, and therefor some points within the stent will become hot-spots, damaging the arterial wall.

Another disadvantage is the fact that the whole stent will be heated and it is not possible to exclude end- or midsections or raise individual sections to different temperatures.

2. *How does your idea address the disadvantages of the current technology? What problems are solved by your idea? What is different from the current technology? What are the advantages of your idea?*

Ferro magnetic materials lose their magnetic properties when raised past a certain temperature called the Curie point. If an alternating magnetic field is used to heat a material, it is clear that the maximum temperature to be reached is the Curie temperature.

If one would incorporate an RF acceptor material with a Curie point equal to the most desired treatment temperature to prevent restenosis in a stent design(as described above), one would be able to overcome most or even all of the disadvantages as described above. By applying a remote RF field, one would be able to raise the temperature of the stent without having the necessity of monitoring and controlling the temperature, due to the Curie effect.

In case of a metal stent one could either disperse such material as a powder through a polymer coating to be added to the surface of the stent. One could also coat different regions of the stent using different powders with different Curie temperatures or coat only parts of the stent. To prevent the stent to be heated up by the effect decribed in the article from the AHA, one could align the magnetic field or the patient as such that the integral of the magnetic field lines passing through the stent would be zero, causing the change in magnetic flux to be zero. By choosing different RF frequencies one could choose such a frequency that would have the most heating effect on the FeO powder while having minimal effect because of the changing flux. One could also apply a rotating alternating magnetic field which in only part of the rotation would heat through the changing flux.

In case of a polymer stent, one could build in the powder either in the stent material or within a coating as described above without having the heating effect due to the changing flux. Again one could choose to use different powders with different Curie temperatures in different regions of the stent.

The idea has become feasible with the commercial availibility of such material by a company called Triton http://www.tritonsys.com/smartbond.html . They produce FeO powders with diameters in the order of 1 to 10 micrometer (but are working on much smaller diameters)

3. Alternatives: Describe any alternative designs, methods of construction or operation or manufacturing of the above device or method. For example, are there alternative materials that may be cheaper or that may provide different features such as stiffness? Are there other products or devices that may incorporate the idea? What other features might the idea incorporate? Put yourself in the competitor's shoes... How would you take advantage of this idea but avoid the device or method?

An interesting case is to use this FeO powder in side a memory polymer. One could trigger a stent (or any other medical device) made of this material, to change shape by inducing a higher temperature by applying a RF field to heat the device.

4. What BSC products are affected? What competitor products are affected?

Stents

5. Will the idea be manufactured outside the US? If so, where? Please list any foreign countries you believe BSC should seek patent protection in and why. For example, a competitor manufactures in France or the market potential is highest in Japan.

Everywere

II. General Information

1. Documentation of Idea.

   a. Date of earliest known documentation of idea:
   (Please attach a copy if available.)

      Lab Notebook No. ___ & Page No. ___
      If different, date of first known drawings:
      Who has custody of drawings?

   b. Date of first known internal disclosure:

      (Rich Goodin, Dan Horn)

2. Prototype:
   a. Start date of first known prototype/model build:
   (add any description of the first or other prototypes that may be helpful)
Ordered similar ferro magnetic material from Philips Eindhoven i , but stopped further experimentation

   b. Date of first known test of idea:
      Bench, animal or clinical?
      (add any description of test results that may be helpful)

   c. Please list any witnesses who saw the prototype.

3. What is the current project phase?
(concept, development or scale-up?)

   Product to be released and release date:
   Engineering Project Number:

4. Disclosure outside of BSC:
   a. Has the idea been disclosed outside of BSC?

      If no:
   Is a future disclosure planned? Where and when? (If less than 2 months away, please notify the on-site patent representative immediately.)

   b. If yes:
   Was the disclosure written or oral?
To whom was the disclosure made and why?
   By whom?
   Is a written confidentiality agreement (CDA) in place?

5. Has a prototype or model been used or shipped external to BSC? Has the idea been incorporated in a commercially released product?
   If no, when is a prototype expected to be used or shipped external to BSC and when is a product expected to be commercially released? (If less than 2 months away, please notify the on-site patent representative immediately.)

7. Please list any potentially relevant publications, presentations, patents or patent applications or other descriptions of which you are aware:

8. Name any key physicians who might be or are interested in the idea.

Boston Scientific Corporation

Please have the disclosure witnessed by at least one person, preferably two people: one who may not understand the idea and is only witnessing the existence of the disclosure; and one who understands the idea, yet who is not an innovator or directly involved with the project. Each witness should read the disclosure, sign and date the front page of the disclosure and initial each page of the disclosure.

Please attach any other descriptions of the idea, notes, samples, specifications, drawings and prior art that may assist in the development of a patent application. The witnesses should initial each attachment.

Your disclosure will be reviewed by the Patent Review Board, and you will be notified as to the decision to pursue or further develop this idea.

Exhibit B

FAX COVER

Corporate Technology

Fax: (508) 650-8937

Boston Scientific
One Boston Scientific Place
Natick, MA 01760-1537
Tel: (508) 650-8000

Date: ,

Number of pages including cover sheet: 5

TO:	JAN Webber
Fax:	763-494-2111

FROM:	John Holmes
Direct Phone:	(508) 652-5126

REMARKS

☐ Urgent ☐ Reply ASAP ☑ For your review ☐ Please comment

JAN,

Here's The INFO I will TALK WITH YOU LATER AFTER you MEET WITH Tribond.

John

5086508937 PAGE.01

TOXIKON

ISO-9001 Certified

TEST RESULT CERTIFICATE

Sponsor	Boston Scientific Corporation-M125 Natick	**Technical Initiation**	
Address	One Boston Scientific Place Natick, MA 01760	**Technical Completion**	
Contact	John Holmes	**Report Date**	
P.O. Number	830261	**Project Number**	01-4432-N1
		Protocol Reference #	BSC/ISO-MEM-ET/001

Test Article	FK 2-132A	**Ratio**	4 gm per 20 mL
Lot # / Part #	Not Supplied by Sponsor	**Vehicle**	MEM complete
Study	Elution Test – ISO	**Temp/Time**	37°C for 24 hours

REFERENCE: This study was conducted based on the procedure described in the International Organization for Standardization, Biological Evaluation of Medical Devices - Part 5: Tests for *In Vitro* Cytotoxicity, ISO 10993-5, 1999.

GENERAL PROCEDURE: The biological reactivity of a mammallan monolayer, L929 mouse fibroblast cell culture, in response to the test article extract was determined. Extracts were prepared at 37±1°C for 24 hours in a humidified atmosphere containing 5±1% Carbon dioxide. Positive control (natural rubber) and negative control (negative control plastic) articles were prepared to verify the proper functioning of the test system. The test article or control article extracts were used to replace the maintenance medium of the cell culture. All cultures were incubated in triplicate for 48 hours, at 37±1°C, in a humidified atmosphere containing 5±1% Carbon dioxide. Biological reactivity (cellular degeneration and malformation) was rated on a scale from Grade 0 (No Reactivity) to Grade 4 (Severe Reactivity). The test article met the requirements of the test if none of the cultures exposed to the test article showed greater than a Mild Reactivity, Grade 2.

RESULTS: No signs of reactivity (Grade 0) were exhibited by the cell cultures exposed to the test article extract or the negative control article extract at the 48 hour observations. Severe reactivity (Grade 4) was observed for the positive control article extract at the 48 hour observation.

CONCLUSION: The test article is considered non-cytotoxic and meets the requirements of the Elution Test, ISO 10993-5.

AUTHORIZED PERSONNEL:

Leigh Waugh-Cohen, B.A.
Study Director

Felice Randi LaMadeleine, B.S.
Quality Assurance

CONFIDENTIAL

15 Wiggins Avenue • Bedford, Massachusetts 01730
(781) 275-3330 • E-mail: www.toxikon.com

CONFIDENTIAL

HEMOLYSIS *IN VITRO* DATA SHEET

TYPE OF SAMPLE: Resin DESCRIPTION: FIC2-132A 50% MnZn Ferrite 50% Polaris 6333

PART NO. 1000160-01 LOT NO. N/A REV. N/A

NATURE OF SAMPLE: ( ) LIQUID (X) SOLID ( ) OTHER: _____

START DATE: _____ COMPLETION DATE: _____ ROOM TEMP: 70°F

TYPE OF TEST: (X) USP ( ) MODIFIED (X) EXTRACT ( ) DIRECT CONTACT

TYPE OF BLOOD: (X) RABBIT ( ) HUMAN (X) CITRATE ( ) HEPARIN LOT NO. 17281 EXP.

(X) 0.9% SALINE LOT NO. 0318 EXP. _____ ( ) 0.9% PREPARED

( ) DIRECT CONTACT METHOD

CUT/MEASURED/WEIGHED: DATE: _____ BY: _____ AMOUNT : R1 _____ R2 _____ R3 _____

NEGATIVE CONTROL: WEIGHT OF POLYPROPYLENE PELLETS: R1 _____ R2 _____ R3 _____

(X) EXTRACTION METHOD

DATE EXTRACTED: _____ BY: Rick Bourne

CUT/MEASURED/WEIGHED: DATE: _____ BY: RB AMOUNT: R1 5.00429 5.00489 R2 _____

(X) 70 ± 2°C, 24 HRS ± 30 MIN ( ) OTHER: _____

EXTRACT APPEARANCE: (X) CLEAR ( ) TURBID ( ) OTHER: _____

EXTRACTION CONTROLS

NEGATIVE CONTROL: WEIGHT OF POLYPROPYLENE PELLETS: 5.00849

POSITIVE CONTROL: ( ) 0.1% $NaCO_3$ LOT NO. _____

(X) 0.1% $NaCO_3$ PREPARED

INCUBATION

(X) 65 MIN ± 5 MIN AT 37 ± 2°C

CENTRIFUGATION

TIME: (X) 10 MIN ( ) OTHER: _____

RCF: (X) 500 x G ( ) OTHER: _____

CONFIDENTIAL

HEMOLYSIS *IN VITRO* RESULT SHEET

UV/VIS OD READING

READING: WAVELENGTH: (x) 540 NM ( ) OTHER: _____

SAMPLE IDENTIFICATION	REP # 1 (NM)	REP # 2 (NM)	REP # 3 (NM)	AVERAGE (NM)
TEST SAMPLE	0.043	0.045	0.054	0.047
POS. CONTROL	1.048	0.924	0.880	0.95
NEG. CONTROL	0.025	0.029	0.018	0.024

FORMULA & CALCULATION

$$\% \text{ HEMOLYSIS} = 100 \times \frac{T - N}{P - N} \qquad \frac{0.023}{0.926}$$

WHERE: T = TEST SAMPLE OD
N = NEG. CTR. OD
P = POS. CTR. OD

RESULTS:

TEST SAMPLE = 2.5 % HEMOLYSIS

INTERPRETATION OF RESULTS

IF THE AVERAGE HEMOLYSIS VALUE IS 5% OR LESS, THE MATERIAL IS CONSIDERED NON-HEMOLYTIC. NEGATIVE PERCENT HEMOLYSIS IS EQUIVALENT TO ZERO HEMOLYSIS.

COMMENTS:

Q.A. ANALYSIS: Rich Bore DATE: _____

Q.A. REVIEWER: Paulene Machado DATE: _____

WHEN SURFACE AREA CANNOT BE DETERMINED DUE TO THE CONFRIGURATION OF THE SPECIMENT, USE 0.1 G OF ELASTOMERS OR 0.2 G OF PLASTIC OR OTHER POLYMERS FOR EVERY 1 ML OF EXTRACTING FLUID.

HEAVY METALS AS LEAD
DATA AND RESULT SHEET

TYPE OF SAMPLE: Resin (1000160-01) DESCRIPTION: 1 50% MN2N Resin 50% Pebax 6333

PART NO. FK2-132A LOT NO. N/A REV. N/A

NATURE OF SAMPLE: ( ) LIQUID (X) SOLID ( ) OTHER: _____

START DATE: COMPLETION DATE: ROOM TEMP: 20°C

TYPE OF TEST: (X) USP ( ) MODIFIED

CUT/MEASURED/WEIGHED: DATE: BY: RB AMOUNT: 6.0030 g

EXTRACTION TIME: 9:00AM TEMP: 70°C BY: Rick Bowe

EXTRACTION APPEARANCE: (X) CLEAR ( ) TURBID ( ) OTHER: _____

TEST DATE	COLOR OBSERVATION		TEST RESULTS		PASS/FAIL
	BLANK	SAMPLE	>1PPM	≤ 1PPM	
	med Brown	Clear		✓	Pass

COMMENTS: developmental stages

CONFIDENTIAL

Q.A. ANALYST: Rick Bowe DATE:

Q.A. REVIEWER: Pauline Machado DATE:

****
*** TX REPORT ***
****

TRANSMISSION OK

TX/RX NO	4870
CONNECTION TEL	919782504533
CONNECTION ID	TRITON SYSTEMS I
ST. TIME	
USAGE T	
PGS. SENT	4
RESULT	OK